UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,538	03/26/2001	Zuomei Li	106101.144	6847

32254 7590 02/01/2007

KEOWN & ASSOCIATES
500 WEST CUMMINGS PARK
SUITE 1200
WOBURN, MA 01801

EXAMINER	
EPPS FORD, JANET L	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/817,538	LI ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 October 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

2. The drawings filed 10-31-06 by Applicants are accepted by the Examiner.

Response to Arguments

3. The rejection of claims 1-3, and 7 under 35 U.S.C. 102(e) as being anticipated by Besterman et al. (US Patent No. 6,953,783.); and the rejection of claims 1-3, 5 and 7 under 35 U.S.C. 103(a) as being unpatentable over Besterman et al. as applied to claims 1-3 and 7 above, in view of Bennett et al. (1996, see PTO-892 mailed 8/06/2002, Reference "U"), are withdrawn in response to Applicant's arguments.

Claim Rejections - 35 USC § 112

4. Claims 1-3, and 5 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the prior Office Action. (Written Description).

5. Applicant's arguments filed 10-31-06 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that one skilled in the art would clearly understand that Applicant's had possession of the full scope of the antisense oligonucleotide encompassed by the instant claims. Moreover, Applicants

argue that the specification as filed is fully enabled in regards to the instantly claimed invention, and that even though effective antisense molecule must be found empirically does not necessarily make the experimentation undue.

As stated in the prior Office Action, although Applicants provide a means for testing the ability of a putative oligonucleotide to inhibit one or more human deacetylase isoforms, apart from further experimentation, the skilled artisan would not have been able to predict the structures of the full scope of the claimed oligonucleotides encompassed by the instant invention. According to MPEP § 2163, providing a method for isolating the claimed invention is not evidence of description.

6. Moreover, contrary to Applicant's assertions, applicant's have not adequately described what structural characteristics are required to possess the claimed specific function, namely those that inhibit one or more specific human histone deacetylase isoforms selected from the group consisting of HDAC-1, HDAC-2, HDAC-3, HDAC-4, HDAC-5, HDAC-6, HDAC-7, and HDAC-8, and furthermore the other human isoforms known in the art, but less than all histone deacetylase isoforms, wherein said histone deacetylase isoforms include those selected from all species which encode this enzyme, as well as all allelic and polymorphic variants of these enzymes. It is noted that the specification as filed includes only antisense compounds that hybridize to the Human form of these enzymes (see Table 1).

Additionally, Applicants disagreed with the examiner's interpretation of the claims as encompassing antisense compounds that hybridize to DNA or RNA or undefined length. Contrary to Applicant's assertions, the instant claims recite wherein the claimed

oligonucleotide is about 15 to about 26 nucleotides in length and hybridizes to "**a region** *(of undefined length)* of RNA or double-stranded DNA that encodes **a portion** *(of undefined length)* of HDAC-1. " Although the length of the claimed oligonucleotide is defined to some extent (note the term "about" is not specifically defined), the structural requirements for hybridization to "a region" that encodes "a portion" of HDAC-1 remains broad and inadequately described.

As stated in the prior Office Action, Branch (1998) states that "[b]ecause it is very difficult to predict what portions of an RNA molecule will be accessible *in vivo*, effective antisense molecules must be found ***empirically*** by screening a large number of candidates for their ability to act inside cells." (page 49, col. 1, paragraph 3).

Since it is apparent that further experimentation is required to identify the full scope of the compounds encompassed by the instant claims, it remains that the Applicants were not in possession of the full scope of the claimed invention at the time of filing.

Double Patenting

7. Claims 1-3, and 5 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application No. 10/870,587, for the reasons of record. Applicant's arguments filed

Claim Rejections - 35 USC § 103

8. Claims 1-3, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schreiber et al. (WO 97/35990 A2) in view of Bennett et al. (1996, see PTO-892 mailed 8/06/2002, Reference "U").

Schreiber et al. describe the design of antisense oligonucleotides of at least 12 nucleotides in length, that hybridizes under stringent conditions to at least 12 consecutive nucleotides of SEQ ID NO: 1-4 of Schreiber et al. SEQ ID NO: 1 of this reference encodes a histone deacetylase that comprises a sequence that is 99.4 % identical to nucleotides 111 through 1559 of SEQ ID NO: 2 of the instant application. Due to the high level of sequence similarity between the histone deacetylase gene (HD1) of Schreiber et al. and HDAC-1 (SEQ ID NO: 2) of the instant application, antisense oligonucleotides that are complementary to HD1 of the prior art, would necessarily be complementary to HDAC-1 of the instant application.

The antisense oligonucleotides of Schreiber et al. function to specifically hybridize under cellular conditions with cellular mRNA or genomic DNA encoding one or more of the histone deacetylase genes so as to inhibit the expression of this gene by inhibiting transcription or translation (see page 5, lines 8-28). The antisense oligonucleotides are preferably modified oligonucleotides, which are resistant to endogenous nucleases, and comprise for example phosphoramidate, phosphorothioate and methylphosphonate analogs of DNA or peptide nucleic acids (see page 27, lines 25-35).

Schreiber et al. does not disclose the limitation about 15 to about 26 nucleotides in length, since the term "about" is not adequately defined, absent evidence to the contrary the antisense compounds of Schreiber et al. described above meet this limitation.

Schreiber et al. does not disclose wherein the antisense compounds are chimeric or hybrid, or furthermore comprises the specific 2'-O-methyl modifications recited in claim 1.

According to Bennett et al. (1996; antisense compounds designed wherein the terminal nucleotides comprise 2'-O-methyl modifications, and further comprising an internal unmodified region, have increased nuclease stability, increased potency, and enhanced pharmacokinetic properties, in comparison with unmodified antisense compounds (see page 38, 1st paragraph).

It would have been obvious to the ordinary skilled artisan at the time of the instant invention, to modify the antisense compounds of Schreiber et al. to comprise the modification as recited in the instant claimed. Absent evidence to the contrary, the ordinary skilled artisan would have been motivated to make the claimed modified oligonucleotides since the prior art teaches that these modifications are known to enhance the properties of these compounds in a cellular environment, for example increase nuclease stability as described above.

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford, Ph.D.
Primary Examiner
Art Unit 1633

JLE